REMARKS

The Examiner is thanked for the due consideration given the application. This amendment is being filed concurrent with a Request for Continued Examination.

Claims 1-12 and 16-24 are pending in the application. Claim 4 has been amended to improve the language in what is believed to be a non-narrowing fashion. Claims 16-24 are newly presented. New claims 16-20 find support in the specification at page 14, lines 14-16. New claim 21 generally sets forth subject matter from claims 1 and 11. New claims 22-24 generally correspond to subject matter found in claims 5-7.

No new matter is believed to be added to the application by this amendment.

Rejection Under 35 USC §103(a)

Claims 1-12 remain rejected under 35 USC §103(a) as being unpatentable over ELLIOTT et al. (WO 0100047). This rejection is respectfully traversed.

The present invention pertains to a method of reducing the serum levels in a mammal of at least one of a) cholesterol; b) low density lipoprotein (LDL) cholesterol relative to high density lipoprotein (HDL) cholesterol; c) low density lipoprotein (LDL) cholesterol; d) very low density lipoprotein (VLDL) cholesterol; e) apolipoprotein B; and f) triglycerides. The method of the present invention includes orally administering

to a mammal a composition comprising β-casein where the β-casein is comprised of at least 95% β-casein A^2.

First, it is noted that he European Patent Office has issued an official communication indicating its intention to grant a patent on the equivalent European application. The allowed claims related to β-casein for use in the treatment of hypercholesterolemia, hyperlipidemia and atherosclerosis by reducing the serum level in a mammal of any one or more of: cholesterol, LDL cholesterol relative to HDL cholesterol, LDL cholesterol, VLDL cholesterol, apolipoprotein B and triglycerides, where the β-casein is formed of at least 95% β-casein A.

The European Patent Office has also considered Elliott et al., which is cited by the Official Action. Elliott et al. describe that a reduction of vascular diseases can occur through two distinct mechanisms: the use of tHcy-reducing agents to directly counter tHcy induced vascular damage; and by reducing the incidence of diabetes, by providing bovine milks high in the A^2 variant of β-casein owing to the exclusion of the A^1 and B variants. This is not a statement of any positive effect of β-casein A but rather a statement about excluding β-casein A^1.

The present invention is based on the first demonstration that administering β-casein A^2 has a positive therapeutic effect, which is not just related to the exclusion of β-casein A^1. This is not taught or suggested by the prior art.

The Official Action maintains the rejection over ELLIOT et al. The Official Action states that "Elliott et al. discloses a method for reducing cardiovascular disease and peripheral vascular disease comprising the steps of manufacturing and administering a dietary supplement in the form of a milk product including A^2 β-casein but substantially no A^1 or B β-casein." The Official Action further states that Elliott et al. disclose that the milk comprising β-casein A^2 can be optionally formulated with tHcy-reducing compounds that will reduce diabetes and vascular disease. The Official Action considers that a skilled person would recognize that the tHcy-reducing compounds are added to further enhance the beneficial effects of β-casein A^2.

The Official Action further states that "the functional limitation and/or the mechanism of how it does what it does is not relevant since the ingested β-casein A^2 has the overall effect of reducing diabetes and coronary heart disease."

In response, the applicant reiterates that Elliott et al. fail to disclose or suggest that β-casein A^2 lowers serum levels of cholesterol, LDL cholesterol, VLDL cholesterol, apolipoprotein B and triglycerides. The applicant reiterates that the effect of β-casein A^2 on the serum levels could not be predicted from the disclosure of Elliott et al.

The Official Action suggests that Elliott et al. disclose that β-casein A^2 can be provided as a supplement to reduce cardiovascular disease (lines 307-311). However, Elliott

et al. disclose a method for reducing the incidence of Type I diabetes, Type 2 diabetes, cardiovascular disease, cerebrovascular disease, peripheral vascular disease, and/or degeneration of blood vessel walls by providing a dietary supplement in the form of a milk product including β-casein A^2 but substantially no β-casein A^1 or B, ***fortified by*** addition of another compound which is a tHcy-reducing agent. tHcy-reducing compounds can reduce a patient's homocysteine levels, thereby reducing the risk of cardiovascular disease.

Homocysteine is well established in medical and scientific literature as a risk factor or predictor of heart disease that is independent of other reported risk factors, such as serum levels of cholesterol, LDL cholesterol relative to HDL cholesterol, LDL cholesterol, VLDL cholesterol, apolipoprotein B or triglycerides. For example, one of the mechanisms by which homocysteine may be a risk factor is by imparting vascular damage through the generation of superoxide and hydrogen peroxide. (These compounds may be related to damage to the arterial endothelium.)

The "principles" described by Elliott et al. on page 12 do nothing more than suggest that β-casein A^1 or β-casein B is correlated with Type I diabetes, whereas β-casein A^2 is not. There is no statement of any positive effect of β-casein A^2 on diabetes, let alone on the serum levels of cholesterol, LDL

cholesterol, VLDL cholesterol, apolipoprotein B and triglycerides.

In contrast, the present invention is based on the first demonstration of positive therapeutic effects from administering β-casein A^2. This is not just related to the prophylactic effect of the exclusion of β-casein A^1 as described in the prior art. The cited prior art document does not teach or suggest that a positive effect can be gained from administering β-casein A^2.

The Official Action considers that the elements of reducing cholesterol, apolipoprotein, triglycerides, hypercholesterolemia, hyperlipidemia and atherosclerosis are correlated with an increased risk of heart disease; that Elliott et al. disclose a method for reducing the incidence of cardiovascular disease by administering β-casein A^2 and that it would therefore be reasonable to expect that those elements would be reduced upon administration of β-casein A^2. However, the applicant reiterates that not only do Elliott et al. fail to teach or infer such a reduction in these elements, but that Elliott et al. ***teach away*** from any such influence. For example, Elliott et al. discuss that the reduction of vascular diseases is "directly through the use of tHcy-reducing agents" and "indirectly by reducing the incidence of diabetes through (a) provisional bovine milks high in the A2 variant of β-casein and

low in Al and B variants, and/or (b) exploitation of the immunological properties of β-casomorphin 9".

A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). A *prima facie* case of obviousness may also be rebutted by showing that the art, in any material respect, teaches away from the invention. *In re Geisler*, 116 F.3d 1465, 1471, 43 USPQ2d 1362, 1366 (Fed. Cir. 1997).

The applicant reiterates that vascular disease and diabetes have many contributing factors and physiological indicators. Therefore, it cannot be said that the skilled person would predict a reduction of these specific elements, based on what is disclosed by Elliott et al.

Referring to the Official Action's comments about the disclosure on page 24 of Elliott et al., the applicant again notes that there is nothing in this disclosure that points the skilled person to a reduction in the serum levels of cholesterol, LDL cholesterol, VLDL cholesterol, apolipoprotein B and triglycerides. This, together with the teachings of Elliott et al. that *teach away* from predicting such a reduction in the serum levels, means that Elliott et al. cannot be said to suggest such a reduction.

Also, at page 3, the Official Action asserts that the elements of reducing cholesterol, apoliproprotein, triglycerides, hypercholesterolemia, hyperlipidemia and atherosclerosis would occur to one of ordinary skill in light of the single reference of ELLIOT et al. However, the Official Action fails to point out where in the single reference of ELLIOT et al. itself a teaching or inference of these elements resides.

To establish a *prima facie* case of unpatentability, "the prior art reference (or references when combined) must teach or suggest all the claim limitations." *MPEP* §2143. In addition, if a reference needs to be modified to achieve the claimed invention "there must be a showing of a suggestion or motivation to modify the teachings of that reference to the claimed invention in order to support the obviousness conclusion." *Sibia Neurosciences Inc. v. Cadus Pharmaceutical Corp.*, 225 F.3d 1349, 55 USPQ2d 1927 (Fed. Cir. 2000).

It is thus clear that one of ordinary skill and creativity could not with any certainty have predicted from Elliott et al., that administration of β-casein A^2 would reduce serum levels of cholesterol, LDL cholesterol relatived to HDL cholesterol, LDL cholesterol, VLDL cholesterol, apolipoprotein B or triglycerides.

One or ordinary skill and creativity would thus fail to produce a claimed embodiment of the present invention from a

knowledge of ELLIOT et al., and a *prima facie* case of unpatentability has thus not been made.

Further, even if one assumes *arguendo* that unpatentability could be alleged, this unpatentability is fully rebutted by the unexpected results of the present invention. These unexpected results are evidenced by the experimentation on rabbits set forth at pages 15-27 of the specification. For example, the effects of the present invention on the average intima to media ratios (indicative of arterial thickening) are set forth in Figure 1 of the application, which is reproduced below.

Figure 1

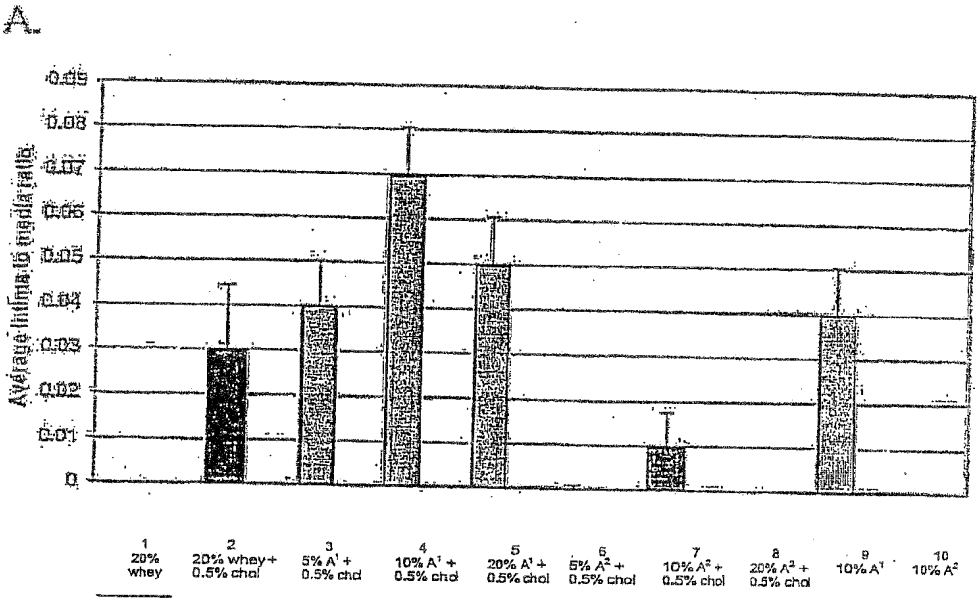

Table of Significance (P<0.05)

Group	Is significantly different from Group
1	3, 4, 5
2	1, 5, 8, 10
3	1, 6, 8, 10
4	1, 6, 8, 10
5	1, 6, 8, 10
6	3, 4, 5
7	3, 4, 5
8	3, 4, 5
9	1, 6, 8, 10
10	3, 4, 5

Figure 1 shows that groups fed β-casein A^2 (both with and without added cholesterol) has smaller neointimal thickenings that their β-casein A^1 fed counterparts. See specification at page 14, lines 1-6.

These unexpected results thus fully rebut any unpatentability that can be alleged from ELLIOT et al.

This rejection is believed to be overcome, and withdrawal thereof is respectfully requested.

Conclusion

Prior art cited but not utilized is believed to be non-pertinent to the instant claims.

The objections and rejections are believed to have been overcome, obviated or rendered moot and that no issues remain. The Examiner is accordingly respectfully requested to place the application in condition for allowance and to issue a Notice of Allowability.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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